

Amendments to the Specification:

Please replace the following new paragraph entered by Preliminary Amendment filed February 9, 2004 on page 1, immediately following the title:

--The present application is a continuation application of ~~PCT/EP02/08963, filed August 9, 2002~~ and PCT/EP02/08963, filed August 9, 2002, which claims priority to European Patent Application No. 01119377.8, filed August 10, 2001, European Patent Application No. 01119528.6, filed August 14, 2001, and U.S. Provisional Patent Application No. 60/315,955, filed August 31, 2001 the teachings of each of which are hereby incorporated by reference.--

Please replace the paragraph beginning at page 29, line 28, with the following:

--The DNA fragment spanning the C/T₋₁₃₉₁₀ variant was amplified using one biotinylated (5'-Bio-CCTCGTTAATACCCACTGACCTA-3'; SEQ ID NO:9) primer and unbiotinylated (5'-GTCACCTTTGATATGATGAGAGCA-3'; SEQ ID NO:8) primer. For G/A₋₂₂₀₁₈ biotinylated (5'-Bio-TGCTCAGGACATGCTGATCAA-3'; SEQ ID NO:13) and one unbiotinylated (5'-CTACCCTATCAGTAAAGGCCTA-3'; SEQ ID NO:12) primer were used under conditions described above. 10 µl of the PCR product was captured in a streptavidin coated microtiter well (Lab systems, Finland). The wells were washed, and bound DNA was denatured as described by Syvänen et al. (Am J Hum Genet. (1993), 52, 46-59) and Syvänen and Landegren (Hum Mutat. (1994), 3, 172-9). 50 µl of the minisequencing reaction mixture contained 10 pmoles of the minisequencing primers for C/T₋₁₃₉₁₅ (5'-GGCAATACAGATAAGATAATGTAG-3'; SEQ ID NO:10), G/A₋₂₂₀₁₈ (5'-AAAAACAGCATTCTCAGCTGGGC-3'; SEQ ID NO:14), and 0.1 µl of either H-dCTP, H-dGTP corresponding to the lactase non-persistence allele (115 Ci/mmol; Ammersham, UK) or H-dTTP, H-sATP corresponding to the lactase persistence allele and 0.05 units of DNA polymerase (Dynazyme II, Finnzymes) in its buffer was added to each well. The microtiter plates were incubated for 20 min at 50°C, and the wells were washed. The detection was

eluted, and the eluted radioactivity was measured in a liquid scintillation counter (Rackbeta 1209, Wallac, Finland). Two parallel minisequencing reactions were carried out for each PCR product.--

Please replace the paragraph beginning at page 31, line.19, with the following:

--To monitor for the prevalence of the hypolactasia-associated variant in the Finnish population a solid-phase minisequencing method^{19,20} was used to screen DNA samples of 938 anonymous Finnish blood donors originating either from the Western early settlement region or the Eastern late settlement region of Finland (Table 4). Experimentally, the DNA fragment spanning the C/T.₁₃₉₁₀ variant was amplified using one biotinylated (5'-CCTCGTTAATACCCCTGACCTA-3'; SEQ ID NO:9) primer and unbiotinylated (5'- GTCAC TTTGATATGATGAGAGCA-3'; SEQ ID NO:8) primer. For G/A.₂₂₀₁₈ we used one biotinylated (5'- AGTCTGTGGCATGTGTCTTCATG-3'; SEQ ID NO:15) and one unbiotinylated (5'- TGCTCAGGACATGCTGATCAACT-3'; SEQ ID NO:16) primer under conditions described above. 10 µl of the PCR product was captured in a streptavidin coated microtitre well (Lab system, Finland). The wells were washed, and the bound DNA was denatured as described previously^{19,20}, 50 µl of the minisequencing reaction mixture contain 10 pmoles of the minisequencing primers for G/A.₂₂₀₀₅ (5'- GACAAAGGTGTGAGCCACCG-3'; SEQ ID NO:17), G/A.₁₃₉₁₅ (5'-GGCAATACAGATAAGATAATGTAG-3'; SEQ ID NO:10) and 0,1 µl of either H-dCTP corresponding to the lactase non-persistence allele (115 Ci/mmol; Amersham, UK) or H-dTTP corresponding to the lactase persistence allele and 0.05 units of DNA polymerase (Dynazyme II, Finnzymes) in its buffer was added to each well. The microtiter plates were incubated for 20 min at 50 °C, and the wells were washed. The detection primer was eluted, and the eluted radioactivity was measured in a liquid scintillation counter (Rackbeta 1209, Wallac, Finland). Two parallel minisequencing reactions were carried out for each PCR product. The overall prevalence of the putative hypolactasia genotype CC-₁₃₉₁₀ (170 cases) was 18.1%, with higher prevalence (16.8% versus 18.9%) in the western than in the eastern sample (Table 4).

These values are in good agreement with the epidemiological study reporting the prevalence of 17% among Finnish speaking Finns with an increasing gradient from West to East². The same set of samples for the G/A₂₂₀₁₈ polymorphism was also genotyped, and the LD between these two SNPs monitored using the D' statistic²¹. They were found to be in almost complete LD ($D' = 0.98$, $p = 7.62 \times 10^{-11}$, Table 5).--

Please cancel the present "SEQUENCE LISTING", pages 1-9, submitted for PCT/EP02/08963, and insert therefor the accompanying paper copy of the Substitute Sequence Listing, page numbers 1 to 8, at the end of the application.